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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
08/716,209	10/09/96	PRADIER	~~L ST94014 US~~

EXAMINER

ART UNIT	PAPER NUMBER
~~GUEKER, S~~ 1817	11

1SN2/1125

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DATE MAILED: 11/25/97

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☑ Responsive to communication(s) filed on 9/2/97

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☑ Claim(s) 27-54 is/are pending in the application.
Of the above, claim(s) 42-47 & 51-54 is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☑ Claim(s) 27-41 & 48-50 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☑ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☑ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
☑ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been
☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☑ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of Reference Cited, PTO-892
☑ Information Disclosure Statement(s), PTO-1449, Paper No(s). 4 & 7
☐ Interview Summary, PTO-413
☑ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

–SEE OFFICE ACTION ON THE FOLLOWING PAGES–

DETAILED ACTION

1. The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1817.

2. Applicant's election with traverse of Group I, claims 27-41 and 48-50 in Paper No. 10 is acknowledged. The traversal is on the ground(s) that the special technical feature of the instant invention is that it is a defective adenovirus encoding BDNF, and that Barde does not teach nor fairly suggest a defective recombinant adenovirus. This is not found persuasive because the specification defines "defective" adenovirus as simply adenovirus "deleted of certain viral regions" (page 4, line 3), which may be accomplished by substituting "the DNA sequence encoding BDNF" for viral sequences (sentence bridging pages 9-10). Barde discloses the substitution of DNA that encodes BDNF in an adenovirus, in addition to such manipulations of DNA as promoter/enhancer elements and marker genes that would inherently entail the deletion of certain viral regions of the adenovirus, if only to make room for the splicing in of restriction sites by which the DNA encoding BDNF or other heterologous DNA could be inserted into the adenoviral genome.

The requirement is still deemed proper and is therefore made FINAL.

3. Claims 30 and 36 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the

invention. The specification does not contain an adequate written description, examples, or guidance on genomic DNA (gDNA) sequences for BDNF being used in an adenovirus. The specification only teaches cDNA sequences encoding BDNF for the adenovirus. The skilled artisan would be faced with undue experimentation without a reasonable expectation of success in making a recombinant adenovirus with a gDNA sequence because it is unpredictable how the artisan would solve the problem of non-coding introns when using a viral vector to produce a protein product in the absence of regulatory and splicing controls that would normally be present in a specialized cell like a neuron or glial cell that normally produced the final protein product, in this case, BDNF.

4. Claims 27-29, 31-34, 37-41, and 48-50 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a cDNA encoding BDNF (or a precursor protein) that is adequately characterized by chemical or structural characteristics, does not reasonably provide enablement for any substance or derivative that may be named "brain-derived neurotrophic factor." The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The term "BDNF" carries no chemical or structural limitation to the recited chemical product, but only a functional limitation (neurotropism) and a source limitation (brain-derived). As such, the claims encompass any manner of substance that the brain produces that can be neurotrophic, such as neurotransmitters, adhesion molecules, even extracellular fluid (saline), etc. that are not envisioned by the instant specification. A protein's function cannot be

adequately predicted from its amino acid structure, so any "derivative" of BDNF produced by adding, deleting, or substituting amino acids would be unpredictable in regards to the desired properties of BDNF. It is suggested that the BDNF encoded by the adenovirus vector of the instant claims recite some chemical or structural limitations to keep the breadth of the claims commensurate with the disclosure.

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 27-29, 31, and 48 are rejected under 35 U.S.C. 102(b) as being anticipated by Barde et al. ("Barde"). Barde discloses an adenovirus encoding human prepro/BDNF cDNA and transfected mammalian cells (column 18, line 32 to column 20, line 53, and column 38, line 7 to column 40, line 18).

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 32-35, 37-41, and 48-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Barde in view of Le Gal La Salle. The teachings of Barde are as set forth in ¶6 above. Barde did not teach specialized viral promoters for the nervous system. Le Gal La Salle discloses replication deficient adenovirus vectors for gene transfer into neurons and glia that use RSV-LTR promoters and GFAP (page 988). It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the BDNF of Barde and the adenovirus techniques of Le Gal La Salle in order to treat diseases of the nervous system amenable to BDNF treatment as suggested by Barde.

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen Gucker whose telephone number is (703) 308-6571. The examiner can normally be reached on Mondays through Thursdays from 0730 to 1800.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Paula Hutzell, Ph.D., can be reached on (703) 308-4310. The fax phone number for this Group is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

SG

Stephen Gucker

November 24, 1997

PAULA K. HUTZELL
SUPERVISORY PATENT EXAMINER
GROUP 1800